INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005596

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 G01N33/68 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, PAJ, EMBASE, CHEM ABS Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CALVO ROSA MARIA ET AL: "Immunohistochemical and morphometric studies of the fetal pancreas in diabetic pregnant rats. Effects of insulin administration" ANATOMICAL RECORD, vol. 251, no. 2, June 1998 (1998-06), pages 173-180, XP002332470 ISSN: 0003-276X page 179 ----- -/--	1-3,5, 7-17,22, 23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 June 2005	11. 10. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Durrenberger, A

3

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005596

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PIETILAEINEN T ET AL: "THE IMPORTANT PROGNOSTIC VALUE OF KI-67 EXPRESSION AS DETERMINED BY IMAGE ANALYSIS IN BREAST CANCER" JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, SPRINGER INTERNATIONAL, BERLIN, DE, vol. 122, no. 11, 1996, pages 687-692, XP008028143 ISSN: 0171-5216 the whole document	1-3,5, 7-17,22, 23
Y	GERLACH C ET AL: "PROLIFERATION-ASSOCIATED KI-67 PROTEIN IS A TARGET FOR AUTOANTIBODIES IN THE HUMAN AUTOIMMUNE DISEASE SYSTEMIC LUPUS ERYTHEMATOSUS" LABORATORY INVESTIGATION, UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY, BALTIMORE,, US, vol. 78, no. 1, January 1998 (1998-01), pages 129-130, XP002073106 ISSN: 0023-6837 the whole document	1-3,5, 7-17,22, 23
Y	COROMINOLA H ET AL: "Identification of novel genes differentially expressed in omental fat of obese subjects and obese type 2 diabetic patients" DIABETES, NEW YORK, NY, US, vol. 50, no. 12, December 2001 (2001-12), pages 2822-2830, XP002293068 ISSN: 0012-1797 abstract	1-3,5, 7-17,22, 23
Y	"CLONTECH.PCR-Select differential screening kit. User Manual" CLONTECH, 10 September 2001 (2001-09-10), pages 1-35, XP002307356 pages 4-7; figure 3	1-3,5, 7-17,22, 23
Y	SURWIT R S ET AL: "Differential effects of fat and sucrose on the development of obesity and diabetes in C57BL/6J and AJ mice" METABOLISM, CLINICAL AND EXPERIMENTAL, W.B. SAUNDERS CO., PHILADELPHIA, PA, US, vol. 44, no. 5, May 1995 (1995-05), pages 645-651, XP004540280 ISSN: 0026-0495 cited in the application the whole document	1-3,5, 7-17,22, 23

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3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005596

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LIM H W ET AL: "Identification of differentially expressed mRNA during pancreas regeneration of rat by mRNA differential display" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 299, no. 5, 20 December 2002 (2002-12-20), pages 806-812, XP002324520 ISSN: 0006-291X the whole document	1-3,5, 7-17,22, 23
Y	BERNAL-MIZRACHI E ET AL: "GENE EXPRESSION PROFILING IN ISLET BIOLOGY AND DIABETES RESEARCH" DIABETES/METABOLISM RESEARCH AND REVIEWS, WILEY, LONDON,, GB, vol. 19, no. 1, 2003, pages 32-42, XP008045358 ISSN: 1520-7552 the whole document	1-3,5, 7-17,22, 23
Y	WO 00/66787 A (OHIO UNIVERSITY; KOPCHICK, JOHN, JOSEPH; TIONG, JEAN) 9 November 2000 (2000-11-09) the whole document	1-3,5, 7-17,22, 23
P,X	SONE H ET AL: "Pancreatic beta cell senescence contributes to the pathogenesis of type 2 diabetes in high-fat diet-induced diabetic mice." DIABETOLOGIA. JAN 2005, vol. 48, no. 1, January 2005 (2005-01), pages 58-67, XP002332471 ISSN: 0012-186X the whole document	1-3,5, 7-17,22, 23
P,Y	WO 2004/092419 A (OHIO UNIVERSITY; KELDER, BRUCE; KOPCHICK, JOHN, J) 28 October 2004 (2004-10-28) the whole document	1-3,5, 7-17,22, 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/005596

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-23 are directed to a method of treatment of the human/animal body, or to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 3, 5, 7-17, 22, 23 (all partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-23 are directed to a method of treatment of the human/animal body, or to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1, 3, 5, 7-17, 22, 23 (all partially)

A method for protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of a polypeptide or an expression vector encoding such, the polypeptide being substantially structurally identical or conservatively identical in sequence to the mouse protein having accession number CAA58026.1;
A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to the mouse protein having accession number CAA58026.1.

Inventions 2-58: claims 1, 3, 5-17, 22, 23 (all partially)

A method for protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of a polypeptide or an expression vector encoding such, the polypeptide being substantially structurally identical or conservatively identical in sequence to one of the 58 remaining mouse proteins listed in subtable 1A;
A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to one of the 58 mouse proteins listed in subtable 1A.

Inventions 59-228: claims 2, 4, 6-23 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method for protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of an antagonist or an antisense of a polypeptide which is substantially structurally identical or conservatively identical in sequence to one of the 169 mouse proteins listed in subtable 1B;
A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of an "unfavorable" human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to one of the 169 mouse proteins listed in subtable 1B.

Inventions 229-249: claims 1-4, 7-23

A method for protecting a human subject from progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises administering to the subject a protective amount of a polypeptide, or an expression vector encoding it, or an antagonist or antisense thereof, the polypeptide being substantially structurally identical or conservatively identical in sequence to one of the 21 mouse proteins listed in subtable 1C;
A method of screening for human subjects who are prone to progression from a normoinsulinemic state to a hyperinsulinemic state, or from either to a type II diabetic state, which comprises assaying tissue or body fluid samples from said subjects to determine the level of expression of a "favorable" or "unfavorable" (i.e. "mixed") human marker gene encoding a human protein which is substantially structurally identical or conservatively identical in sequence to one of the 21 mouse proteins listed in subtable 1C.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/005596

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0066787 A	09-11-2000	CA 2370134 A1	09-11-2000
WO 2004092419 A	28-10-2004	NONE	